REMARKS

Amendments

Claims 11, 30 and 31 have been canceled, claims 27 and 28 have been withdrawn, claims 1-4, 10, 12-18, 20, 22, 26 and 29 have been amended, and claim 32 has been added. Upon entry of the amendment, claims 1-10, 12-26, 29 and 32 will be pending. Support for the added claims can be found in the specification, for example, on page 13, lines 1-20; the Examples; the Figures; and in the claims as originally filed.

The foregoing amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Rejections

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-10, 12-26 and 29-31 stand rejected as allegedly failing to comply with the written description requirement. The Examiner argues that the claims encompass a large genus of targeting constructs comprising a regulator comprising any protein or DNA sequence arranged in any fashion on the construct. As noted by the Examiner, the regulator must function to down regulate expression of the selection marker if the construct does not insert into the target sequence.

The claims as amended are drawn to a targeting vector capable of modifying or disrupting a target gene through homologous recombination, comprising:

(a) a first sequence capable of homologously recombining with a first region of a target gene;

(b) a second sequence capable of homologously recombining with a second region of the target gene;

(c) a selectable marker cassette comprising a DNA sequence encoding a positive selection marker, said cassette located between the first sequence and second sequence; and

(d) a regulator sequence encoding an element capable of repressing expression of the DNA sequence encoding the selection marker; said regulator sequence located adjacent to the first sequence or second sequence, on a side opposite of the selectable marker cassette;

where homologous recombination of the first sequence and second sequence with the target gene results in expression of the selection marker; and where random insertion of the vector into the target gene results in repression of the DNA sequence encoding the selection marker. Applicant submits that the regulator sequence is defined both functionally (repressing expression of the selectable marker sequence) and spatially (located adjacent to either the first and second sequence, and outside the marker cassette) such that, upon homologous recombination with the target sequence, the regulator sequence is lost and the selection marker is expressed. Upon random integration, the regulator sequence is retained and the expression of the selection marker is repressed. It is submitted that the specification fully supports the spatial arrangements of the vector elements.

Applicant respectfully submits that the written description requirement is satisfied and requests withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-25 and 29-31 stand rejected on the ground of indefiniteness. The Examiner argues that the term "regulator" is indefinite. The Examiner suggests amending the claims to clarify whether a protein or nucleotide sequence is intended.

The claims have been amended to recite "a regulator sequence encoding an element capable of repressing expression of the DNA sequence." As contemplated by the amended claim language, the encoded element can be either a protein or a nucleotide sequence. It has been clarified that the vector itself comprises a regulator sequence.

Claim 1 has been rejected on the ground that "target gene" lacks clear antecedent basis. The preamble of the claim has been amended to clarify the basis for the term.

Claims 12 and 13 have been rejected for reciting "wherein the regulator comprises at least one repressor sequence." Claim 12 has been amended to specify that the repressor element is a protein.

Claims 20, 22, 29 and 30 stand rejected for reciting "the regulator controls expression of a selectable marker." The claims have been amended to recite dependency on claim 1.

Applicant submits that the claims as amended address the Examiner's concerns. Withdrawal is respectfully requested.

Rejection under 35 U.S.C. § 102(b)

Claim 26 stands rejected as anticipated by Capecchi, which is cited as teaching methods of gene targeting using positive-negative selection markers.

Claim 26 has been amended to recite dependency on new claim 32 which recites a vector wherein the marker cassette comprises the lac operator and the regulator sequence encodes for a lac repressor protein. Homologous recombination would result in retention of a lac operator between the homologous arms. Capecchi does not teach such a target cell.

Withdrawal is respectfully requested.

Claims 1, 18, 20, 29 and 30 stand rejected as being anticipated by Kuebler, which is cited as disclosing the vector pDK H436am. The Examiner argues that the H436am mutation is a selectable marker cassette.

The claims have been amended such that the selectable marker cassette comprises DNA encoding a positive selection marker. The claimed vector also comprises a regulator sequence encoding an element capable of repressing expression of the DNA sequence encoding the selection marker. Kuebler does not disclose either element as set forth in the amended claims.

Withdrawal of the rejection is respectfully requested.

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2725.

Respectfully submitted,

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Date

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